UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/034,950	12/26/2001	Bhami Shenoy	A2039-9000	9344

37462 7590 12/05/2008

LOWRIE, LANDO & ANASTASI, LLP
ONE MAIN STREET, SUITE 1100
CAMBRIDGE, MA 02142

EXAMINER	
KIM, ALEXANDER D	

ART UNIT	PAPER NUMBER
1656	

NOTIFICATION DATE	DELIVERY MODE
12/05/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

docketing@ll-a.com
gengelson@ll-a.com

Office Action Summary	Application No.	Applicant(s)	
	10/034,950	SHENOY ET AL.	
	Examiner	Art Unit	
	ALEXANDER D. KIM	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 August 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *95-135* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *95-135* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/06/2008;8/29/2003*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Application Status

1. In response to the previous Office action, a non-Final rejection (mailed on 02/12/2008), Applicants filed a response and amendment received on 08/12/2008. Said amendment cancelled Claims 1-94; and added new Claims 95-135.

Claims 95-135 are pending in the instant Office action and will be examined herein.

Information Disclosure Statement

2. The missing page of information disclosure statement (IDS) filed on 11/06/2008 has been reviewed, and its references have been considered. A copy of Form PTO/SB/08 is attached to the instant Office action.

Withdrawn-Compliance with Sequence Rules

3. The previous non-compliance with Sequence Rules, because six amino acid sequences listed under "N-terminal sequence" on page 108 without appropriate SEQ ID NOs, is withdrawn by virtue of Applicants' amendment.

Withdrawn-Claim Objections

4. The previous objection of Claims 91 and 94 is withdrawn by virtue of cancelling Claims 91 and 94.

Withdrawn-Objections to the Specification

5. The previous objection to the specification, because the abstract of the disclosure filed on 3/25/2002: (a) is not on a separate page in accordance with 37 CFR 1.52(b)(4); (b) has more than one paragraph; and (c) has more than 25 lines/250 worlds; is withdrawn by virtue of new Abstract filed on 8/12/2008.

Withdrawn-Claim Rejections - 35 USC § 112

6. All previous rejection of Claims 86-94 are rejected under of 35 U.S.C. 112, second paragraph, is withdrawn by virtue of cancelling Claims 86-94.

7. The previous rejection of Claims 84, 85, 91 and 94 are rejected under 35 U.S.C. § 112, first paragraph, written description, by virtue of applicants' cancelling Claims 84, 85, 91 and 94; and the recited term "infliximab" is interpreted as limited to the Remicade™ in view of recitation of instant specification [i.e., "Infliximab is a chimeric murine/human monoclonal antibody commercially available as Remicade™ (Centocor, Leiden, the Netherlands)].

Claim Objections

8. Claims 96, 106 and 126 recite "wherein the pH is 8.6" or "wherein the pH is 8.5". In order to substantially improve claim form, it is suggested that applicant amend claims

Claim Rejections - 35 USC § 112 – 1st paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

New Matter

9. Claims 100-104, 110-114, 120-124 and 130-135 are rejected under 35 U.S.C. 112, first paragraph, **new matter**, as failing to comply with the written description requirement. The claim(s) contain subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 100-104 recite "16.67 mg/ml" for infliximab, "23.3%" for ethoxyethanol, "0.13 M" for lithium sulfate and/or "0.067 M" for Tris buffer; Claims 110-114 recite "16.67 mg/ml" for infliximab, "26.67%" for PEG-400, "0.13 M" for lithium sulfate and/or "0.067 M" for Tris buffer; Claims 120-124 recite "37.88 mg/ml" for infliximab, "15.15%" for PEG MME 550, "0.091 M" for calcium chloride, and/or "0.076 M" for Tris HCl; and Claims 130-135 recite "6.67 mg/ml" for infliximab, "13.3%" for PEG 300, "0.067 M" for Tris buffer, "3.33% for PEG 8000" and/or "6.67%" for glycerol; wherein recitation of said concentrations are not supported by the original disclosure.

According to applicant's remarks at p. 12, "The new claims are supported by the application as filed, *e.g.*, Examples 34-37 at pages 98-99". The only apparent support for the noted limitations is in the preparation of the crystallization solution. For example, at p. 98, paragraph [0274], the specification discloses "mixing 50 µl of antibody (50

mg/ml) with 100 µl of 35% ethoxyethanol, 0.2 M lithium sulfate, 0.1 M Tris, pH 8.6. In this example, the calculated infliximab concentration in this example is 16.66666666.... mg/ml which is different from 16.67 mg/ml; the calculated ethoxyethanol concentration in this example is 23.333333.... % which is different from 23.3 %; the calculated lithium sulfate concentration in this example is 0.1333333... M which is different from 0.13 M; and the calculated Tris concentration in this example is 0.06666666.... M which is different from 0.067 M. Thus, the calculated concentrations do not correspond to the recited concentrations. The applicant is advised to point out the support in the original disclosure or amend the instant claims.

10. Claims 95-135 are rejected under 35 U.S.C. § 112, first paragraph, written description, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The rejection was stated in the previous office action as it applied to previous Claims 84, 85, 91 and 94. In response to this rejection, applicants have cancelled Claims 1-94; and traverse the rejection as it applies to the newly added claims. Applicants argue that new claims 95-135 satisfy the written description requirements for the crystals and methods recited therein which are clearly described in the Examples 34-37 at pages 98-99, such that possession of the claimed subject matter is clear.

Applicants' arguments have been fully considered but are not deemed persuasive for the following reasons. The examiner acknowledges that applicants were in possession of four species of infliximab crystals encompassed by the genus of claimed crystals and the methods recited in the instant specification on pages 98-99. However, because the genus of claimed infliximab crystals and methods of making said crystals therein are widely varying, these four disclosed representative species of infliximab crystals fail to show possession of all members of the genus for the reasons stated below.

The Court of Appeals for the Federal Circuit has recently held that a "written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as be structure, formula [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." University of California v. Eli Lilly and Co., 1997 U.S. App. LEXIS 18221, at *23, quoting Fiers v. Revel, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) (bracketed material in original). To fully describe a genus of genetic material, which is a chemical compound, applicants must (1) fully describe at least one species of the claimed genus sufficient to represent said genus whereby a skilled artisan, in view of the prior art, could predict the structure of other species encompassed by the claimed genus and (2) identify the common characteristics of the claimed molecules, e.g., structure, physical and/or chemical characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or a combination of these (Enzo Biochem 63 USPQ2d 1609 (CAFC 2002)).

Initially, it is noted that the recited term "infliximab" has been interpreted according to the specification's disclosure at p. 98, paragraph [0272], which states, "Infliximab is a chimeric murine/human monoclonal antibody commercially available as RemicadeTM. (Centocor, Leiden, the Netherlands). This monoclonal antibody has been widely used to treat rheumatoid arthritis and Crohn's disease. Infliximab is a chimeric IgG1 kappa immunoglobulin that binds to the TNF-A antigen. It is composed of murine light- and heavy-chain variable region sequences and a human constant region sequence. The Infliximab antibody has an approximate molecular weight (MW) of 149 kD". The instant specification teaches four infliximab compositions as described in Examples of 34-37. However, the genus of claimed crystals and methods includes infliximab (i.e., Remicade^{TM}) crystals (or methods of crystallizing infliximab) comprising any constituent(s) as long as the crystal has any concentration (or any pH) of (a) ethoxyethanol, lithium sulfate and Tris buffer; (b) PEG-400, lithium sulfate, and Tris Buffer; (c) PEG MME 550, calcium chloride and Tris HCl buffer; or (d) PEG 300, Tris buffer, PEG 8000, and glycerol. The dependent claims 96, 98-104, 106, 108-114, 116, 118-124, 126 and 128-135 recites a specific pH OR a concentration of at least one constituent, the pH OR the concentration(s) of the constituents are unlimited. The instant specification discloses very specific concentration and pHs of constituents in four infliximab crystals. The prior art does not teach any other representative species of infliximab crystals (or a method of forming said crystal thereof) encompassed by the genus of the claims. As noted in a previous Office action (*e.g.*, pp. 6-8 of the Office action mailed on 2/26/07), it is not only the constituents of a crystallization solution that

are critical to achieving crystallization. It is also the concentration of each of these elements AND the pH of the crystallization solution. Thus, the instant specification alone or in combination with the prior art also does not describe sufficient species for the claimed genus for one skilled in the art to possess the claimed inventions; and does not describe the correlation between the constituents (concentration and pH) in claimed infliximab crystals (or a method of forming said crystal thereof) with the "function" of crystallization of said infliximab. In order for a broad generic claim to satisfy the written description requirement, the specification must provide adequate description in the specification to reflect the variation in the genus by describing a sufficient number of representative species. In Regents of the University of California v. Eli Lilly & Co. the court stated:

> "A written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." Fiers, 984 F.2d at 1171, 25 USPQ2d 1601; In re Smythe, 480 F.2d 1376, 1383, 178 USPQ 279, 284985 (CCPA 1973) ("In other cases, particularly but not necessarily, chemical cases, where there is unpredictability in performance of certain species or subcombinations other than those specifically enumerated, one skilled in the art may be found not to have been placed in possession of a genus ...") Regents of the University of California v. Eli Lilly & Co., 43 USPQ2d 1398.
> Thus, the species which are described in the specification are not deemed to be

representative of the entire genus of antibody crystals and methods for which the claims are drawn to because these representative species fail to reflect the wide variation among the members of the genus. For the reasons above and reasons stated in the previous office actions, the Claims 95-135 are rejected under 35 USC 112, first paragraph, for written description.

11. Claims 95-135 are rejected under 35 U.S.C. 112, first paragraph, scope of enablement, because the specification, while being enabling for antibody crystals of infliximab as prepared according to Examples 34-37 on pages 98-99; does not reasonably provide enablement for all crystals (or a method of forming said crystal thereof) as broadly encompassed by the claims comprising the recited constituent(s) having any concentration AND pH of (a) ethoxyethanol, lithium sulfate and Tris buffer; (b) PEG-400, lithium sulfate, and Tris Buffer; (c) PEG MME 550, calcium chloride and Tris HCl buffer; or (d) PEG 300, Tris buffer, PEG 8000, and glycerol. The dependent claims 96, 98-104, 106, 108-114, 116, 118-124, 126 and 128-135 recite a specific pH OR concentration, however, is unlimited with respect to at least element of pH AND/OR concentration.

The rejection was stated in the previous office action as it applied to previous scope of enablement rejections for Claims 84-94. In response to this rejection, applicants have cancelled Claims 1-94; and traverse the rejection as it applies to the newly added claims.

Applicants argue that new claims 95-135 satisfy the enablement requirements for the crystals and methods recited therein which clearly described in the Examples 34-37 at page 98-99, such that applicants clearly enables making and using the full scope of the claimed subject matter without undue experimentation as suggested in the previous office action at pages 8, 10 and 15.

Applicants' arguments have been fully considered but are not deemed persuasive for the following reasons. The examiner acknowledges that applicants are enabled for four species of infliximab crystals encompassed by the claimed crystals and the methods recited in the instant specification on pages 98-99. However, as noted above, the scope of crystals and methods encompasses crystals with any concentration AND/OR pH of the constituents of the crystal or crystallization solution and in view of the breadth of the claims, the state of the art, the high level of unpredictability, and the amount of experimentation required, undue experimentation is required to make and use the full scope of claimed crystals and methods for the reasons stated below.

The factors to be considered in determining whether undue experimentation is required are summarized *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). The Court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (Wands, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (Wands, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state

of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. While all of these factors are considered, a sufficient amount for a *prima facie* case are discussed below.

12. The breadth of the claims: Claims 95-135 are drawn to an infliximab crystal (or a method of forming said crystal thereof) with at least the recited components and having any concentration OR pH of (a) ethoxyethanol, lithium sulfate and Tris buffer; (b) PEG-400, lithium sulfate, and Tris Buffer; (c) PEG MME 550, calcium chloride and Tris HCl buffer; or (d) PEG 300, Tris buffer, PEG 8000, and glycerol. The dependent claims 96, 98-104, 106, 108-114, 116, 118-124, 126 and 128-135 are drawn to an infliximab crystal having any other constituents recite a specific pH OR concentration of at least one constituent, however, is unlimited with respect to at least element of pH AND/OR concentration.

The nature of the invention: The invention is related to antibody crystals of infliximab, also known commercially as Remicade™ (assuming the brand name antibodies has not been modified over time) and a method of forming said crystal thereof as shown in the Examples 34-37 on pages 98-99; wherein the infliximab is dissolved in a solution containing 500 mg sucrose, 0.5 mg polysorbate 80, 2.2 mg monobasic sodium phosphate and 6.1 mg dibasic sodium phosphate prior to setting up crystallization. Three infliximab crystals have used tumbling of crystallization solution to make infliximab crystal. However, the ability to crystallize a given antibody (or protein) was, at the least, challenging to a skilled artisan as even minor alterations in the

conditions of crystallization could result in failure to form a crystal of infliximab as described below.

The state of the prior art; The level of one of ordinary skill; and The level of predictability in the art: In the instant case, as previously noted in non final office action mailed on 5/15/2006, the quantity of experimentation would be considerable because the smallest change in ***any*** parameter in crystallizing a protein/antibody can have enormous consequences. Thus, it is not enough to have the crystallization conditions of a related/similar protein/antibody or 'native' protein/antibody. Rather, what would be required is precise instruction about how to make the each and every crystal (each and every one) in order to avoid undue experimentation. However, there is no direction or guidance in the specification of how a skilled artisan might achieve crystal growth of Infliximab in any conditions (having any other molecule or peptide, for example) or with any other crystallization techniques (e.g. hanging drop, sitting drop, capillary liquid-liquid diffusion etc.). The nature of the invention and of the prior art suggests that crystallizing proteins is an extremely tenuous science; what works for one protein or antibody does not necessarily for another, and what works for one native protein or antibody does not necessarily work for a mutant or fragment even though they essentially contain the same protein/antibody that has already been crystallized. Specific crystallization conditions (e.g. temperature, buffer, salt, protein concentration etc.) are needed for each protein and/or antibody (see Weber, Overview of Crystallization Methods. Methods in Enzymology, 1997, Vol. 276, pp. 13-22, as cited previously).

At best, the art of crystallization is unpredictable even to those skilled in the art who may either perform the experiments by hand or who are assisted by automated robotics because it often times requires thousands of individual experiments in order to find the one or two conditions that are successful. Even then, there is no guarantee. It is even a well known fact in the art that luck often times play a fortuitous role in obtaining successful crystallization conditions despite the extremely high skill level of those in the art. For example, Drenth describes a case where it seemed impossible to successfully crystallize a particular protein they were working on until the air conditioner in the laboratory broke down over night thereby increasing the temperature in the lab to the "correct temperature" which was needed to induce successful crystal growth (see Drenth, "Principles of Protein X-Ray Crystallography", 2nd Edition, 1999 Springer-Verlag New York Inc., Chapter 1, p. 19, 4th paragraph, lines 1-2, as cited previously). This is just one example out of the many countless tales of the unpredictability of the art. As cited previously on pages , Klyushnichenko (Curr. Op. Drug Discovery, 2003, 6(6):848-54) teaches (p. 849, 1st column, 2nd paragraph, as cited previously):

> The objectives of a bulk protein crystallized process are to rapidly purify and concentrate the produce with high yield and without loss in potency. However, crystallization has not been used widely in the purification or formulation of biological compounds. *This is due to the difficulties in developing crystallization conditions that are reproducible and scalable at clinical- and commercial-scale*."
>
> As discussed above, there are several examples of large-scale protein crystallization; however, researchers frequently report that no clear understanding of the protein crystallization mechanism has yet emerged. Typically several hundred experiments must be performed to determine crystallization conditions, such as pH, buffer type, precipitant type and protein concentration. To control costs and improve efficiency, it is important to minimize the number of experiments, especially if the final or intermediate conditions are to be scaled-up.

Thus, the crystallization of protein (including antibody) is difficult and unpredictable and the number of experimentation required to make and use the claimed invention is high.

The amount of direction provided by the inventor; The existence of working examples: The specification discloses only four working example of the claimed crystal of infliximab and the method of crystallization thereof. See specification pages 98-99. Prior art does not teach the crystallization of infliximab having composition recited in claims. Other than these four working examples, the specification and prior art fail to provide guidance for altering the crystallization conditions for crystallizing infliximab comprising any constituent(s) (e.g., any small molecules or any polypeptide) as long as the crystal have any concentration (or any pH) of (a) ethoxyethanol, lithium sulfate and Tris buffer; (b) PEG-400, lithium sulfate, and Tris Buffer; (c) PEG MME 550, calcium chloride and Tris HCl buffer; or (d) PEG 300, Tris buffer, PEG 8000, and glycerol.

The quantity of experimentation needed to make or use the invention based on the content of the disclosure: While methods of protein crystallization were known at the time of the invention, these methods are specific to a particular protein or antibody. Thus, a skilled artisan is left to experiment by a trial and error process to determine whether the disclosed crystallization conditions can be applied to crystallization of infliximab with any other constituents such as any small molecule or any protein such that infliximab can be crystallized under a different set of crystallization parameters.

In view of the overly broad scope of the claims, the lack of guidance and working examples provided in the specification, the high level of unpredictability as evidenced by the prior art, and the amount of experimentation required to make all methods and crystals as broadly encompassed by the claims, undue experimentation would be necessary for a skilled artisan to make and use the entire scope of the claimed invention.

Thus, applicant has not provided sufficient guidance to enable one skilled in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims. The scope of the claims must bear a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Withdrawn-Claim Rejections - 35 USC § 102/103

13. The previous rejection of Claim 85 under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Ely et al. (Biochemistry, 1978, 17(5):820-23) as evidenced by Chayen (2004, Current Opinion in Structural Biology, 2004, 14: 577-583) is withdrawn by virtue of cancelling Claim 85. Ely et al. also do not anticipate or render obvious the newly added claims because they teach the

crystal of a human IgG2(k) immunoglobulin (Zie) which is different from the crystal of infliximab.

Withdrawn-Double Patenting

14 The previous provisional rejection of Claims 84, 85, 91 and 94 on the ground of nonstatutory double patenting over claims 35 and 41 of U. S. Patent Application No. 10/741,861 since the claims, if allowed, would improperly extend the "right to exclude" already granted in the patent; is withdrawn by virtue of cancelling Claims 84, 85, 91 and 94. The amended claims are also not subject to a provisional rejection in view of the added limitations (i.e., ethoxyethanol, PEG-400, PEG MME 550 and PEG 300) in claims 95, 105, 115 and 127, respectively, since the claims of this application are not anticipated or rendered obvious by the claims of co-pending application 10/741,861.

Conclusion

15. Claims 95-135 are not allowed for the reasons identified in the numbered sections of this Office action. Applicants must respond to the objections/rejections in each of the numbered section in this Office action to be fully responsive in prosecution.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ALEXANDER D. KIM whose telephone number is (571)272-5266. The examiner can normally be reached on 11AM-7:30PM.
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached on (571) 272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a

USPTO Customer Service Representative or access to the automated information

system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Alexander D Kim/
Examiner, Art Unit 1656

/David J. Steadman/
Primary Examiner, Art Unit 1656